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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,274	02/02/2001	Mireille Lamberty	A33595-PCT USA	3555

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BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,274	LAMBERTY ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/1/03, 10-18-2 and 11-25-02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22 and 46* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,22 and 46* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11-16-00* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

Applicants' preliminary amendment filed 2 February 2001, which cancels claims 21 and 45 and amends claims 4-5, 6, 8-17, 22-23, 26, 29-30, 35, 38-40, 43-44 and 46, the amendment filed 18 October 2002, which amends claim 1, the amendment filed 25 November 2002, which amends claims 1, 5-6, 11-12 and 16, and amendment filed 1 August 2003, which cancels claims 23-44 and amends claims 2-20, 22 and 46 have been entered. Also, applicants' petition for extension of time of two months (filed 1 August 2003) has been entered. Claims 1-20, 22 and 46 are pending.

Foreign Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on April 15, 1998. It is noted, however, that applicants have not filed a certified copy with translation of the application France98/04933 as required by 35 U.S.C. 119(b).

Election/Restrictions

Applicants' election of Group I, claims 1-20, 22 and 46 (see Paper filed 18 October 2002) and additional election of the polypeptide encoded by nucleotide 1 to 132 of polynucleotide sequence SEQ ID NO:2 (see Paper filed 1 August 2003 15) with traversal for patent examination is acknowledged. The traversal is on the ground(s) that the claimed polypeptide (Group I) and polynucleotide (Group II) encoding the polypeptide thereof represent a single invention concept (see page 3 of Paper filed 18 October 2002).

Applicants contest the current application has unity in view of formula I structure of claim 1 and commend on the Hoffman et al. peptide wherein the equivalent of Xad does not read

on the formula I thereof (see pages 10-11 of the amendment filed 1 August 2003 and page 5 the last paragraph of Paper filed 18 October 2003). Thus, applicants infer that the application claim 1 is novel and Groups I and II fall into a single inventive concept.

Applicants' arguments have been fully considered but they are unpersuasive because of the reasons as follows. The instant claim 1 recites the open language "consisting essentially of" in the lines where the claim limitation is set forth for Xad, i.e., the current claim language encompasses Xab more than 9 residues. Hoffman et al. peptide is, therefore, reads on the application claim 1. Furthermore, Charlet, M. et al. (*J. Biol. Chem.* (1996) 271, 21808-21813) teach an antimicrobial peptide (*Leiurus* defensin) comprising six cysteine residues and having the structural characteristics set forth in the formula I of claim 1 (see defensin isolated from *Leiurus*, Figure 4, page 21812), e.g., the region (equivalent to Xad of the current application SEQ ID NO:39) of the peptide consists of three amino acid residues. Thus, the lack of unity of the subject matter of the current application stands.

Since applicants have cancelled claims 23-44 (Group II) that is directed to polynucleotide, there appears no basis for arguing the issue regarding a single invention concept represented by the claimed polypeptide (Group I) and polynucleotide (Group II) encoding the polypeptide thereof.

Therefore, elected claims 1-20, 22 and 46 to which the polypeptide encoded by 1-132 nucleotides of the application SEQ ID NO:2 are under examination to the extent that they are drawn to the elected invention.

Specification/Claim Objections

The disclosure is objected to because of the following informalities:

In page 1, line 27, "HIV" should be spelled out in full for the first instance of use. See also page 9, line 11, "PR-1α"; and page 18, line "HPLC".

In page 7, line 7, "SEQ ID NO 2" should be changed to "SEQ ID NO:2". The same change should be made throughout the specification.

In page 32, line 19, "$HPIC_{18}$" is required to be clarified.

In page 33, line 18, "100·C" should be changed to "100 °C". The same change should be made throughout the specification.

In claim 1, "preferably 10", "preferably 9", and "preferably 7" should be changed to "preferably 10 amino acid residues", "preferably 9 amino acid residues", "preferably 7 amino acid residues", respectively. See also claims 5, 7 and 14.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-20, 22 and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation "peptide residue" which is not defined in the specification; the recitation is thus unclear as to whether or not the said residue refers to (a) amino acid residue or (b) a peptide fragment, or a combination of (a) and (b). The dependent claims are also rejected.

Claim 11 is unclear as to "Xag' represents OH"; to what does "OH" refer? Does "OH" mean a hydroxyl group instead of carboxyl group being covalently attached to α-carbon of C-terminal amino acid residue cysteine? In addition, claim 11 recites "a variable residue have a sequence..."; the recitation is unclear as to whether or not the "residue" refers to amino acid residue; given the recited residue as an amino acid, how can a single amino acid residue constitute a peptide sequence?

Claim 12 recites "-Glu-Thr-OH"; the recitation is unclear regarding whether or not the C-terminal carboxyl group (-COOH) is substituted by hydroxyl group "-OH" in the recited dipeptide.

Claim 14 is indefinite in "...targeting in a host organism" wherein the term "targeting" is vague as to what is the object of the said targeting.

Claim 19 is indefinite in "the signal peptide of the tobacco PR-1α gene" because a peptide is structurally distinct from polynucleotide and a signal peptide is a component of a polypeptide precursor, which is subject to posttranslational modification, but not a portion of a gene, *i.e.*, polynucleotide. See also "the signal peptide of the maize polygalacturonase PG1 gene" in claim 19. Suggest "the signal peptide *encoded* by ... gene".

Claim 22 is unclear as to the term "vehicle" which is not defined in the specification. Also, claim 22 is indefinite because claim 22 is directed to the polypeptides that are encoded by non-elected nucleotide sequences of SEQ ID Nos. 1, 3 and 18, which are drawn to non-elected invention and patentably distinct from the elected polypeptide encoded by 1-132 nucleotide of SEQ ID NO: 2. Thus, re-writing the claim is advised in order to eliminate the subject matters which have been withdrawn from consideration in this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-19 and 46 are rejected under 35 U.S.C. 102 (a) as being anticipated by Lamberty M. et al. (*J. Biol. Chem.* (1999) 274, 9320-9326), which is provided by the applicants' IDS.

Lamberty et al. teach an antimicrobial peptide, heliomicine, comprising six cysteine residues and having the structural characteristics set forth in the formula I of claim 1; the Lamberty et al. polypeptide reads on the polypeptide encoded by 1-132 nucleotides of SEQ ID NO:2 of the instant application (see Figure 2, the full-length sequence of 44 residues). Since the the polypeptide of 44 amino acid residues meet every limitations set forth in claims 1-13 and 15-16, the Lamberty et al. anticipates the application claims thereof.

Also, Lamberty et al. teach that the peptide is engineered as a preprosequence by in frame fusion with yeast mating factor MFα1 proregion in order to recombinantly produce the matured peptide in which (see the left column, the second paragraph at page 9324), which meets the limitation set forth in claims 14 and 17-19 of the instant application (note that signal peptide is a component of the recombinant prepropolypeptide or preprolypeptide).

Further, Lamberty et al. teach a method of producing the heliomicin polypeptide comprising culturing the tranformants in which the expression cassette containing polynucleotide

that encodes the polypeptide followed by a large scale purification of the polypeptide thereof from the transformant cells, as applied to claim 46 of the current application.

Claims 1-4, 11 and 15 are rejected under 35 U.S.C. 102 (b) as being anticipated by Charlet, M. et al. (*J. Biol. Chem.* (1996) 271, 21808-21813).

Charlet et al. teach an antimicrobial peptide (*Leiurus* defensin) comprising six cysteine residues and having the structural characteristics set forth in the formula I of claim 1 (see defensin isolated from *Leiurus*, Figure 4, page 21812), e.g., the region (equivalent to Xad of the current application SEQ ID NO:39) of the peptide consists of three amino acid residues.

Charlet et al. teach that the region (equivalent to Xad of the current application SEQ ID NO:39) of the peptide has four basic amino acid residues, i.e., four arginine residues, which meet the limitation set forth in claims 2, 3 and 4 of the instant application.

Charlet et al. teach the region (equivalent to Xaa of the current application SEQ ID NO:39) of the peptide comprises the sequence: X'-Gly-X" wherein X' is NH_2 and X" consists of two residues (Phe-Gly), which meets the limitation set forth in claim 11 (especially directed to the description for Xaa) of the instant application.

Also, Charlet et al. teach that involvement of three intramolecular disulfide bridges in the six cysteine residues of the members of defensin family (see the second paragraph of the left column, page 21810, and, the fourth paragraph of the right column, page 21812), which meets the limitation set forth in the application claim 15.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19, 22 and 46 are rejected under 35 U.S.C. 103(a) as being obvious over Lamberty M. et al. (*J. Biol. Chem.* (1999) 274, 9320-9326) taken with DeRose R. et al. (US Pat. No. 6465719).

Lamberty et al. teach an antimicrobial peptide, heliomicine, comprising six cysteine residues and having the structural characteristics set forth in the formula I of claim 1; the Lamberty et al. polypeptide reads on the polypeptide encoded by 1-132 nucleotides of SEQ ID NO:2 of the instant application (see Figure 2, the full-length sequence of 44 residues). The polypeptide of 44 amino acid residues meet every limitations set forth in claims 1-13 and 15-16.

Also, Lamberty et al. teach that the peptide is engineered as a preprosequence by in frame fusion with yeast mating factor MFα1 proregion in order to recombinantly produce the matured peptide in which (see the left column, the second paragraph at page 9324), which is applied to

claims 14 and 17-19 of the instant application (note that signal peptide is a component of the recombinant prepropolypeptide or preprolypeptide).

Further, Lamberty et al. teach a method of producing the heliomicin polypeptide comprising culturing the tranformants in which the expression cassette containing polynucleotide that encodes the polypeptide followed by a large scale purification of the polypeptide thereof from the transformant cells, as applied to claim 46 of the current application.

Lamberty et al. does not explicitly teach the composition comprising the polypeptide mentioned above.

DeRose at al. teach a peptide sequence of drosomycin (see the patent SEQID NO:15, column 2), which reads on the formula I (SEQ ID NO:39) of the claim 1 of the instant application,

Also, DeRose et al. teach a composition comprising at least one active product having antimicrobial activity, e.g., drosomycin peptide (see column 7, lines 33-43 and the patent claim 21), which is applicable to the application claim 22, and a process of recombinantly producing the drosomycin polypeptide (see column 1, lines 41-50, and column 4, lines 1-67), which meets the limitation of claim 46 of the instant application.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the above reference teachings because (i) Lamberty et al. expressly teach the polypeptide which is the subject matter of the current application, and (ii) DeRose et al. teach the composition comprising the recombinant (fusion) polypeptide (drosomycin) comprising signal peptide, and a process of preparing the polypeptide.

When combined, the above reference teachings would have offered the following favorableness: (**1**) the DeRose et al. composition comprises at least one active product possessing useful broad spectrum of antimicrobial activities, e.g., herbicidal, fungicidal, bactericidal virucidal or insecticidal activity, as taught by DeRose et al. (see column 7, lines 32-36), (**2**) a vector containing the chimeric DNA sequence encoding drosomycin can be transform the subject and thus render the transformant thereof resistant to diseases, in particular of fungal origin, as taught by DeRose et al. (see column 1, lines 58-63), and (**3**) the Lamberty' antifungal peptide has very wide spectrum and specifically targeting on various fungal and yeast strains not bacteria and has the same fungicidal potency at physiological ionic strength (see page 9325, the right column), suggesting a promising application *in vivo* for treating fungus-mediated infection etc. (see the right column, page 982 to page 283, left column, and abstract).

The skilled artisan would have been motivated to combine the above reference teaching to successfully arrive at the current invention with respect to making and using the composition comprising the cysteine-rich antimicrobial polypeptides. Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher

Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

Samuel Wei Liu, Ph.D.
October 17, 2003